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(54) Title: TAXANES COVALENTLY BOUNDED TO HYALURONIC ACID OR HYALURONIC ACID DERIVATIVES

(57) Abstract: The present invention relates to water-soluble taxanes covalently bounded to hyaluronic acid or hyaluronic acid derivatives, and in particular to paclitaxel and docetaxel, useful for the preparation of pharmaceutical compositions to be used in the field of oncology, in the treatment of autoimmune disorders and of restenosis. The invention also relates to the process for preparing taxanes covalently bounded to hyaluronic acid or hyaluronic acid derivatives by direct synthesis between molecules of hyaluronic acid and of taxane or by indirect synthesis by the introduction of a spacer between the hyaluronic acid or hyaluronic acid derivative and the taxane.

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C08B37/00 C08L5/08 A61K47/36 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C08L C08B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EP0-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>LUO Y ET AL: "SYNTHESIS AND SELECTIVE CYTOTOXICITY OF A HYALURONIC ACID-ANTITUMORBIOCONJUGATE" BIOCONJUGATE CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 10, no. 5, 20 September 1999 (1999-09-20), pages 755-763, XP001041280 ISSN: 1043-1802 cited in the application page 755-756</p> <p style="text-align: center;">--- -/--</p>	1-73

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

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Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/11239

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SPARER R. V. ET AL.: "Controlled Release from Glycosaminoglycan Drug Complexes" in "Controlled Release Delivery Systems" 1983, MARCEL DEKKER, NEW YORK XP009025950 page 107-119 page 112-114	1-73
Y	US 4 851 521 A (DELLA VALLE FRANCESCO ET AL) 25 July 1989 (1989-07-25) column 3, line 12-31 column 7, line 61,62 column 13, line 54-61; claim 17	1-73
Y	US 5 648 506 A (SOON-SHIONG P ET AL) 15 July 1997 (1997-07-15) column 2, line 65 -column 3, line 13 column 4, line 19-36; claim 1; example 3	1-73
X	WO 97/33552 A (LI CHUN ;WALLACE SIDNEY (US); YU DONG FANG (US); WALLACE TECH INC) 18 September 1997 (1997-09-18) page 6, line 15 -page 7, line 13; claims 1,12; figure 1A	1-73
A	AKIMA K ET AL: "EVALUATION OF ANTITUMOR ACTIVITIES OF HYALURONATE BINDING ANTITUMORDRUGS: SYNTHESIS, CHARACTERIZATION AND ANTITUMOR ACTIVITY" JOURNAL OF DRUG TARGETING, HARWOOD ACADEMIC PUBLISHERS GMBH, DE, vol. 4, 1996, pages 1-8, XP002942515 ISSN: 1061-186X page 4	1-73
A	US 5 502 081 A (PRESTWICH GLENN D ET AL) 26 March 1996 (1996-03-26) column 11-12	1-73

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claim : 1 (part) .

Conjugate according to claim 1 in which the bond is formed between OH groups of the taxane and carboxyl groups of the hyaluronic acid by means of a spacer (the group of compounds is not unitary, but could be searched without extra effort).

2. Claim : 1 (part)

Conjugate according to claim 1 in which the bond is formed between OH groups of the taxane and carboxyl groups of the hyaluronic acid without spacer.

3. Claim : 1 (part)

Conjugate according to claim 1 in which the bond is formed between OH groups of the taxane and OH groups of the hyaluronic acid.

4. Claim : 1 (part)

Conjugate according to claim 1 in which the bond is formed between OH groups of the taxane and amino groups of deacetylated hyaluronic acid.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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